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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,296	11/14/2003	Tinya Abrams	034536-0680	8864

22428 7590 01/04/2006  
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EXAMINER

WEDDINGTON, KEVIN E

ART UNIT PAPER NUMBER

1614

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/712,296	Applicant(s) ABRAMS ET AL.	
	Examiner Kevin E. Weddington	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 August 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>4-19-04; 8-4-04</u> . | 6) <input type="checkbox"/> Other: _____  |

Claims 1-20 are presented for examination.

Applicants' drawings filed November 14, 2003; and information disclosure statements filed April 19, 2004 and August 4, 2004 have been received and entered.

***Specification***

Applicants may wish to update the statuses of Serial Nos. 10/367,008 and 10/658,801 located on page 33, lines 6 and 10.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 13, 17 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples

- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method of treating cancer comprising administering to a patient in need thereof an effective amount of an indolinone compound of formula I in combination with at least one chemotherapeutic agent.

The state of the prior art, Cecil Reference, Textbook of Medicine, 21 edition (2000), Chapter 198, pages 1060-1074; shows that for the various known cancer types there is no one specific chemotherapeutic agent that is effective for all types of cancer (See Table 198-5 on page 1065, Table 198-6 on page 1066, Table 198-8 on page 1068, and table 198-9 on page 1071).

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown that the instant combination of an indolinone in combination with at least one chemotherapeutic agent is effective to treat all types of cancer.

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The breadth of the claims

The claims are very broad and inclusive to all types of cancer

The amount of direction or guidance provided and the presence or absence of working examples

The working example under Biological Example, shows the instant composition were effective in the inhibition of human breast cancer model, human small cell lung carcinoma, and human colon cancer model.

No working examples of the instant composition to treat or inhibit leukemia, renal cell cancer, thyroid cancer or a neuroendocrine tumor.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the instant composition comprising an indolinone compound of formula I in combination with at least one chemotherapeutic agent is effective in treating all types of cancer. The level of experimentation needed to determine the instant composition would be able to treat all types of cancer is undue. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 1, 13, 17 and 20 are not allowed.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-16 are rendered indefinite and vague by the phrase "at least one chemotherapeutic agent is" followed by a number of agents. Is the chemotherapeutic agent a combination of these agents or a Markush grouping wherein one chemotherapeutic agent is selected from?

Claims 14-16 are not allowed.

To overcome this rejection, the applicants may wish to amend claims 14-16 by inserting this phrase after the word "agent", --selected from the group consisting of--

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each

claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (6,573,293 B2) of PTO-1449 in view of Windholz et al., THE MERCK INDEX, Tenth Edition, 1983, pages 599, 1427 and 1428, abstract nos. 4088, 9784 and 0788; and P.J. Craven, "Platinum Analogs As Potential New Drugs For Bladder Cancer, Urology, 1984, Vol. 23, No., Supplement 3, Reference 41, pp. 54-60.

Tang et al. teach the instant indolinone compounds of formula I are protein kinase inhibitors to treat related cellular disorders such as cancer (See the abstract and column 167, lines 55-64).

The instant invention differs from the cited reference in that the cited reference does not teach the addition of a chemotherapeutic agent as set forth in claims 1, 11, 12 and 14-19. However, the secondary references, Windholz et al. and P.J. Craven, each individually teaches various types of chemotherapeutic agents such as antimetabolites (5-fluorouracil), vinca alkyls (vinblastine and vincristine), and alkylating agents such as platinum (carboplatin, cisplatin and oxaliplatin) are effective in treating various types of cancers. Clearly, one skilled in the art would have assumed the combination of the two individual compounds (an indolinone compound of formula I and chemotherapeutic agents) known to treat or inhibit various types of cancers into a single composition would give an additive effect in the absence of evidence to the contrary.

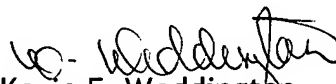
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Claims 1-20 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Kevin E. Weddington  
Primary Examiner  
Art Unit 1614

K. Weddington  
December 20, 2005